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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,297	02/13/2002	Masako Yajima	219451US0	3488

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,297	YAJIMA ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/15/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO REQUEST FOR CONSIDERATION, IDS AND STATUS OF THE CLAIMS

1. The request for reconsideration and the information disclosure statement filed 12/15/05 are acknowledged, entered and considered. Claims 9-32 are now pending in the application. The rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) over the prior art of record are maintained for the same reasons discussed in the previous Office action.

ARGUMENTS ARE NOT PERSUASIVE

CLAIMS REJECTION-35 U.S.C. § 102(b)

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9, 15, 21 and 27 remain rejected under 35 U.S.C. 102(b) as being anticipated by Nitsche (U.S. Patent No. 5,240,909).

Applicant's arguments filed 12/15/05 have been fully considered but they are not persuasive. Applicant has argued that Nitsche ('909) patent is drawn to the use of lactoferrin (Lf) bound to a metal ion, not Lf *per se*, and is drawn to treating endotoxemia, and not a symptom from LPS-induced inflammation. Further, Applicant continues by

stating that Nitsche emphasizes that Lf used **must** have bound either iron or another metal (column 4, lines 15-17). Thus, the Examiner's finding that Nitsche discloses the administration of an effective amount of hLf or animal Lf **as an active agent for suppressing inflammation caused by endotoxin LSP-derived from gram-negative bacteria**, is clearly erroneous. Applicant concludes by stating that the Examiner relies on the disclosure in Example 3 of Nitsche that increase in plasma endotoxin activity was reduced by approximately 58.5% in comparison to an albumin control group by administering Lf. However, the Examiner has ignored the critical fact that the *in vivo* testing in Example 3 involves the use of **Lfs bound to metal ions**, not Lf *per se* is unpersuasive. Contrary to Applicant's arguments, independent claims 9, 15, 21 and 27 are open-ended, in view of the "comprising" and allows for additional ingredient, component or step, and as such, there is no clear indication in the specification or claims to determine the ingredient, component or step included versus excluded, the claims must be read in light of the specification. Since Applicant has failed to establish the exclusion of "Lf bound to a metal ion", and not defined in the instant specification, the claims as drafted are read as "comprising" (i.e., open-ended), and as such Applicant's arguments that Nitsche is drawn to the use Lf bound to a metal ion, not Lf *per se* is unpersuasive. Further, the limitations Applicant argued with (i.e., exclusion of Lf bound to a metal ion) are not recited in the rejected claims. Nevertheless, the claims are interpreted in light of the specification; limitations from the specification are not read into claims. See *In re Geuns*, 988 F.2nd 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, Applicant's argument is not commensurate to the scope of the claims.

Furthermore, as acknowledged on page 3, last paragraph of Applicant's remarks filed 12/15/05 that Nitsche does disclose various *in vitro* experiments in which human and bovine Lf were used in iron-free apoform (column 4, line 37 ff). Among the results disclosed are that when endotoxin is incubated with iron-free apolactoferrin, an average reduction in endotoxin activity of 35.4 to 41.2% is registered, depending on the type and concentration of endotoxin (column 6, lines 17-20) although, the results using Lf with bound metal ion are substantially better (column 6, line 21 ff). Thus, the above acknowledgement clearly shows that Nitsche teaches the use of Lf which is free of a metal ion such as iron-free apolactoferrin (i.e., Lf-0) as well as the use of Lf bound to a metal.

With respect to Applicant's assertion that alleviating a symptom from LPS-induced inflammation is different from treating endotoxemia is unpersuasive. Contrary to Applicant's assertion, as discussed in the previous Office action, the reference of '909 patent discloses the administration of an effective amount of human lactoferrin (hLf) or animal lactoferrin as an active agent for suppressing inflammation caused by endotoxin LPS-derived from gram-negative bacteria, wherein the lactoferrin agent is administered orally or parent rally or enterally (See e.g., abstract, summary of the invention, cols. 10 and 12). Further, it is known in the art that LPS is endotoxin (See e.g., Pub, No.: US 2006/0039921 A1). Endotoxins are pyrogenic (fever-producing substances) and they could be inflammatory and as such they are endotoxic and when they reach the blood stream they are known as endotoxemia (i.e., the presence of endotoxins in the blood). Although, the reference does not disclose alleviating symptoms wherein the symptom is

accumulation of body fluid containing albumin at the inflammation site (claim 9); accumulation of albumin at the inflammatory site (claim 15); decrease of albumin concentration in blood (claim 21); or increase of neutrophils in blood (claim 27). However, on col. 12, lines 61-65, the '909 paten clearly states that when lactoferrin was administered intravenously the initial increase in plasma endotoxin activity—one hour after administration of the antibiotic---was reduced by approx. 58.5% in comparison of the albumin control group. Thus, clearly showing the reduction of albumin concentration in blood, and as such meets the limitation of claim 21. Further, the above conditions/situations are natural occurrence due to the inflammation, and as such it is inherent property of lactoferrin administration to alleviate the symptoms of such condition/situation. Furthermore, as acknowledged by Applicant on page 2, paragraph 2 in the instant specification, it is known in the art that during sepsis caused by gram-negative bacilli, decline in blood albumin concentration, decrease of lymphocytic leukocytes, and increase of neutrophil occur. Also, on page 4, Applicant acknowledges that bovine-type lactoferrin has been used to demonstrate an effect of alleviating various symptoms, which appear after infection. Thus, albumin exudation or increase of blood neutrophils at the inflammatory site, these are expected natural occurrence during inflammation whatever the cause of inflammation is. See also the abstract of Jajima et al (The 4th International Conference on Lactoferrin, Program & Abstract, pp. 77, 1999) which states that lactoferrin, in primary defense system against pathogenic invasion, may play a role in the amelioration of phagocytic activity in PMN through the inhibitory action on LPS-induced TNF α production in neonatal rat *in vivo*. Moreover, in view of *In*

re Sussman, 141 F. 2d 267, 60 U.S.P.Q. 538 (CCPA 1944), the claims are rejected under 35 U.S.C. 102(b) "that since the steps are the same, the results must inherently be the same unless they are due to conditions not recited in the claims." Applicant is claiming an invention employing the **same process steps** but the product(s) is (are) **alleged to be different**. Applicant is required to recite the missing steps to form the alleged different product(s) in view of the above citation. Thus, the prior art discloses the invention substantially as claimed, and as such, anticipates claims 9, 15, 21 and 27 as drafted.

CLAIMS REJECTION-35 U.S.C. § 103(a)

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10-14, 16-20, 22-26 and 28-32 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Nitsche (U.S. Patent No. 5,240,909).

Applicant ahs argued that the Examiner finds that Nitsche discloses the administration of Lf at a dosage of 0.1 mg/g and 300 mg/kg to inhibit endotoxins, relying on the abstract and Example 4. In reply, 0.1 mg is an amount of iron, **not** an amount of Lf; 300 mg is the amount of a solution of bovine-type Lf, **not** the amount of a solution of hLf is not persuasive. Contrary to Applicant's argument, even if 0.1 mg is an amount of iron, not an amount of Lf, however, Applicant acknowledges that 300 mg is the amount of a solution (i.e., comprising Lf, iron and other ingredients) of bovine-type Lf. Thus, in view this acknowledgement and as discussed in the previous Office action, the reference of '909 patent teaches the administration of lactoferrin as an active agent for suppressing inflammation caused by endotoxin LPS-derived from gram-negative bacteria, wherein the lactoferrin is administered at a dosage of 0.1 mg/g and 300 mg/kg to inhibit endotoxins (See e.g., abstract and Example 4) and as such overlaps with the dosage ranges claimed in claims 10-14, 16-20, 22-26 and 28-32 (i.e., 0.1 to 1000 mg/kg). Thus, the reference clearly discloses the administration of lactoferrin as an active agent to suppress inflammation resulting in alleviating symptoms caused from LPS-induced inflammation due to acute inflammation or sepsis of the human by gram-negative bacteria. With respect to the dosage ranges, types of LF and mode of administrations, the ranges, types of Lf and mode of administration disclosed by the

reference and claimed by Applicant overlap in scope as discussed above, and as such, the selection of the appropriate dosages, type of Lf and route of administration would have been *prima facie* obvious because where general conditions of claims are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges or situations by routine experimentation. Further, Applicant's claims are directed to optimization of an "art recognized variable" which is within the purview of one of ordinary skill in the art, *In re Boesch*, 617 F. 2d 272, 205 USPQ 215 (CCPA 1980).

ACTION IS FINAL

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

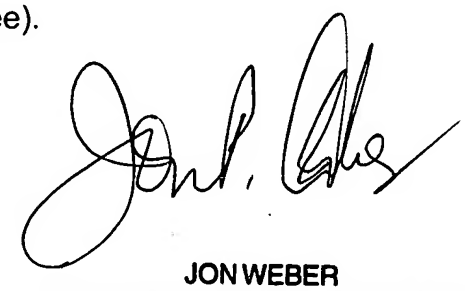
CONCLUSIOIN AND FUTURE CORRESPONDANCE

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, CAMPELL BRUCE can be reached on (571) 272 0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



JON WEBER
SUPERVISORY PATENT EXAMINER

Mohamed/AAM
February 27, 2006